



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|------------------------------|------------------|
| 10/569,077 | 02/21/2006 | David S. Garvey | 102258172US5 | 2613 |
| 25270 7590 01/24/2008 WILMERHALE/NITROMED 1875 PENNSYLVANIA AVE, NW WASHINGTON, DC 20006 | | | EXAMINER HAVLIN, ROBERT H | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1626 | |
| | | | MAIL DATE | DELIVERY MODE |
| | | | 01/24/2008 | PAPER |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|--------------------------------------|--|
| Office Action Summary | Application No. 10/569,077 | Applicant(s) GARVEY ET AL. | |
| | Examiner Robert Havlin | Art Unit 1626 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 November 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) 6-12 and 18-22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 13-17 and 23-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

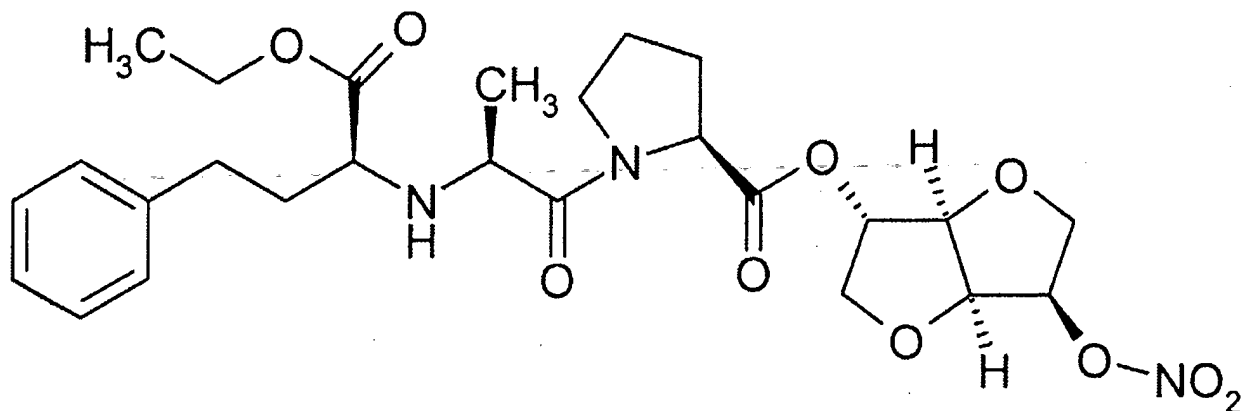
DETAILED ACTION

Status of the claims: Claims 1-25 are currently pending.

IDS: The IDS dated 9/21/07 was considered.

Election/Restrictions

Applicant has corrected an error in their response to the requirement for restriction, thereby changing the elected species following the first action on the merits. For this office action, the examiner will consider the newly elected species of (reading on claims 1-5, 13-17, and 23-25):



As detailed in the following rejection, the elected species was found unpatentable.

Therefore the claims are restricted to only the elected species and the remaining subject matter withdrawn from consideration.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

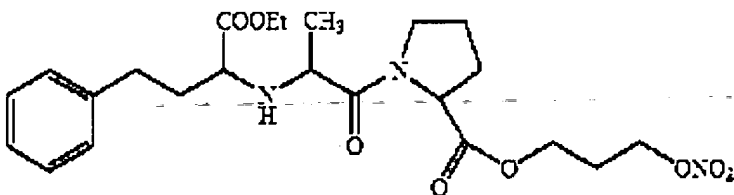
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 1-5, 13-17, and 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 7,217,733 in view of US 6,465,463, PGPUB 2003/0069221 ("221"), Beaumont et al. (Current Drug Metabolism, 2003, 4, 461-485).

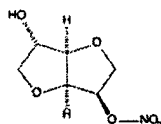
The instant claims read on the elected species.

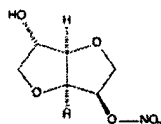
Teaching of the prior art

US 7,217,733 teaches enalapril nitrate derivatives for the treatment of cardiovascular disease. For example, in claim 5 (compound 2) the reference teaches the enalapril nitroxy-propyl ester:



The '733 reference teaches numerous substitutions in place of the nitroxy-propyl ester with the same enalapril core structure as above.



US 6,465,463 teaches Isosorbide mononitrate () in combination with enalapril compounds for the treatment of cardiovascular disease.

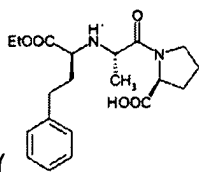
'221 teaches the combination of isosorbide mononitrate with enalapril in addition to the concept of prodrugs.


Beaumont et al. teaches ester prodrug design specifically with enalapril, for example in table 1, page 464. The reference also suggests utilizing the pharmacology of the hydrolysed ester to gain a wanted effect.

Differences between the prior art and the claims

The propyl group of the compound taught by '733 is replaced with isosorbide.

Finding of obviousness



Enalapril () is a well known cardiovascular agent for treating heart disease, commonly known as an ACE inhibitor as described in the instant specification. Isosorbide mononitrate is commonly used to treat cardiovascular disease as is enalapril. The combination of the two for the same purpose to create the elected species would have been obvious to one of ordinary skill in the art. The functionalization of carboxylic acid groups with prodrug agents is well known in the art. The effect of this prodrug approach is: the elected species would separate into the two well known elements of enalapril and isosorbide mononitrate when used as a pharmaceutical. Therefore, one of ordinary skill in the art would immediately recognize the predictable success of attaching isosorbide mononitrate at the carboxylic acid of enalapril to create an ester derivative providing the benefits of both agents when used as a pharmaceutical. Specifically, the '733 patent teaches the functionalization of the carboxylic acid with a nitrate yielding group and '463 teaches the combination with enalapril.

Conclusion

No claim is in condition for allowance. Applicant's amendment of the elected species necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Havlin whose telephone number is (571) 272-9066. The examiner can normally be reached on Mon. - Fri., 7:30am-5pm EST.

If attempts to reach the examiner by telephone are unsuccessful the examiner's supervisor, Joe McKane can be reached at (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Application/Control Number:
10/569,077
Art Unit: 1626

Page 6

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert Havlin/
Robert Havlin, Ph.D.
Examiner
Art Unit 1626

KAMAL SAEED, PH.D.
PRIMARY EXAMINER

Kamal Saeed, Ph.D.
Primary Examiner
Art Unit 1626